

August 18, 1969

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Dear Ernest,

Thank you for your letter. The shock of re-entry that you mentioned was accurate, but we are all functioning by now.

The results of your experiments with "re-denatured" DNA surprised me, not so much because of the absolute increase in hybridization with synthetic RNA, but because of the several fold increase in RNA/DNA ratio on the filter. This means that my figure of about $0.15 \mu\text{g RNA}/\mu\text{g DNA}$ is not correct and may be about 1! In other words, all parts of both strands are transcribed at least to some extent. I was also disappointed in the size of the RNA, which is very small indeed. What the data now adds up to is that under the conditions used, there is considerable random transcription but one strand is favored (accounting for limited self-annealing). There may also be RNase degradation of the RNA.

At the Cold Spring Harbor meeting Henry Westphal reported the synthesis of much larger SV40 RNA which was transcribed entirely (or nearly so) from one strand of SV40 DNA. This RNA was about 4.5×10^5 in molecular weight (DMSO-sucrose gradient); he claimed that some was about 1/2 the MW of SV40 DNA. He used the RNA to separate the SV40 DNA strands by annealing in the presence of excess RNA and separating the DNA-RNA hybrid on Cs_2SO_4 . It was very pretty. In contrast to our conditions for synthesis, he used Burgess' preparation of enzyme, high salt, and very low enzyme to DNA ratio. He did not determine the per cent transcription by hybridization, nor compare in vivo with in vitro RNA.

Yossi Aloni's paper went well. Dulhecco's boys practically read out their earlier comments on the J. Mol. Biol. paper. There was a great deal of interest in the observation. Another interesting paper was Benjamin's selection of host range polyoma mutants using Py-3T3 as permissive host and 3T3 as non-permissive host. He isolated 4 stable mutants and showed that DNA infectivity follows virus infectivity and that all mutants are defective in transformation.

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Basilico had a neat paper on the susceptibility of stable 3T3-BHK hybrids to polyoma infection. The main finding was that cells with balanced mouse and hamster chromosomes are about as permissive as 3T3.

I am setting up to grow SV40 to continue with the DNA-RNA protein attempt. What I plan to do is switch to Westphal's condition to get high molecular weight RNA and see if SV40 proteins are made with this.

Best regards to Leo, Carmela, Bernard and everyone there, and also to Audrey.

Sincerely,

Daniel Nathans

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